WEST Search History

DATE: Tuesday, April 08, 2003

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB; PLUR=YES; OP=OR			
L16	L15 and profilaggrin$	2	L16
L15	L14 and antibod$	967	L15
L14	L13 and (carrier or label$)	979	L14
L13	L12 and "rheumatoid arthritis"	985	L13
L12	L10 and (arginine or citrulline)	4656	L12
L11	L10 and l1	6	L11
L10	L9 or l2 or l3 or l4 or l5 or l6 or l7 or l8	12614	L10
L9	(((424/185.1)!.CCLS.))	1156	L9
L8	(((424/184.1)!.CCLS.))	1665	L8
L7	(((424/184)!.CCLS.))	0	L7
L6	(((530/403)!.CCLS.))	699	L6
L5	(((530/350)!.CCLS.))	9941	L5
L4	(((436/516)!.CCLS.))	243	L4
L3	(((436/506)!.CCLS.))	269	L3
L2	((436/509)!.CCLS.)	138	L2
L1	filaggrin$ or antifilaggrin$	89	L1

END OF SEARCH HISTORY

Connecting via Winsock to Dialog

Logging in to Dialog

Trying 31060000009999...Open

DIALOG INFORMATION SERVICES
PLEASE LOGON:
****
ENTER PASSWORD:
****
Welcome to DIALOG

Dialog level 02.12.60D

Last logoff: 07apr03 12:14:03
Logon file405 08apr03 12:27:07
*** ANNOUNCEMENT ***
***
--File 515 D&B Dun's Electronic Business Directory is now online completely updated and redesigned. For details, see HELP NEWS 515.
***
--File 990 - NewsRoom now contains October 2002 to present records. File 993 - NewsRoom archive contains 2002 records from January 2002-September 2002. To search all 2002 records, BEGIN 990,993 or B NEWS2002
***
--Alerts have been enhanced to allow a single Alert profile to be stored and run against multiple files. Duplicate removal is available across files and for up to 12 months. The Alert may be run according to the file's update frequency or according to a custom calendar-based schedule. There are no additional prices for these enhanced features. See HELP ALERT for more information.
***
--U.S. Patents Fulltext (File 654) has been redesigned with new search and display features. See HELP NEWS 654 for information.
***
--Connect Time joins DialUnits as pricing options on Dialog. See HELP CONNECT for information.
***
--CLAIMS/US Patents (Files 340,341, 942) have been enhanced with both application and grant publication level in a single record. See HELP NEWS 340 for information.
***
--SourceOne patents are now delivered to your email inbox as PDF replacing TIFF delivery. See HELP SOURCE1 for more information.
***
--Important news for public and academic libraries. See HELP LIBRARY for more information.
***
--Important Notice to Freelance Authors--
See HELP FREELANCE for more information
***
For information about the access to file 43 please see Help News43.
***
NEW FILES RELEASED
***Dialog NewsRoom - Current 3-4 months (File 990)
***Dialog NewsRoom - 2002 Archive (File 993)
***Dialog NewsRoom - 2001 Archive (File 994)

***Dialog NewsRoom - 2000 Archive (File 995)
***TRADEMARKSCAN-Finland (File 679)
***TRADEMARKSCAN-Norway (File 678)
***TRADEMARKSCAN-Sweden (File 675)
***
UPDATING RESUMED
***Delphes European Business (File 481)
***
RELOADED
***D&B Dun's Electronic Business Directory (File 515)
***U.S. Patents Fulltext 1976-current (File 654)
***Population Demographics (File 581)
***Kompass Western Europe (File 590)
***D&B - Dun's Market Identifiers (File 516)

REMOVED
***Chicago Tribune (File 632)
***Fort Lauderdale Sun Sentinel (File 497)
***The Orlando Sentinel (File 705)
***Newport News Daily Press (File 747)
***U.S. Patents Fulltext 1980-1989 (File 653)
***TOXNET data is added to ToxFile (F156)

New document supplier
IMED has been changed to INFOTRIE (see HELP OINFOTRI)

>>> Enter BEGIN HOMEBASE for Dialog Announcements <<<
>>> of new databases, price changes, etc. <<<
****
* * * *
SYSTEM:HOME
Cost is in DialUnits
Menu System II: D2 version 1.7.8 term=ASCII
*** DIALOG HOMEBASE(SM) Main Menu ***

Information:
1. Announcements (new files, reloads, etc.)
2. Database, Rates, & Command Descriptions
3. Help in Choosing Databases for Your Topic
4. Customer Services (telephone assistance, training, seminars, etc.)
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7. Data Star(R)

/H = Help /L = Logoff /NOMENU = Command Mode

Enter an option number to view information or to connect to an online
service. Enter a BEGIN command plus a file number to search a database
(e.g., B1 for ERIC).
? b 410

08apr03 12:27:07 User268147 Session D61.1
$0.00 0.160 DialUnits FileHomeBase
$0.00 Estimated cost FileHomeBase
$0.00 Estimated cost this search
$0.00 Estimated total session cost 0.160 DialUnits

File 410:Chronolog(R) 1981-2003/Mar
(c) 2003 The Dialog Corporation

Set Items Description
--- ---- -------
? set hi %%%;set hi %%%
HILIGHT set on as "
HILIGHT set on as "
? b 5, 71, 155, 172
08apr03 12:27:20 User268147 Session D61.2
$0.00 0.070 DialUnits File410
$0.00 Estimated cost File410
$0.04 TELNET
$0.04 Estimated cost this search
$0.04 Estimated total session cost 0.229 DialUnits

SYSTEM:OS - DIALOG OneSearch
File 5:Biosis Previews(R) 1969-2003/Mar W5
(c) 2003 BIOSIS
*File 5: Alert feature enhanced for multiple files, duplicates
removal, customized scheduling. See HELP ALERT.
File 71:ELSEVIER BIOBASE 1994-2003/Apr W1
Set Items Description
S1 72 "PEPTIDYLARGININE DEIMINASE"
S2 863 DEIMINASE?
S3 169 AU='SERRE G' OR AU='SERRE G V' OR AU='SERRE G.' OR AU='SER-
RE GUY'
S4 30 AU='SIMON MICHEL' OR AU='SIMON MICHELE'
S5 0 E 12-36
S6 10 S3 AND S2

6/9/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.

14147807 BIOSIS NO.: 200300141836
cDNA cloning, gene organization and expression analysis of human
peptidylarginine deiminase type I.
AUTHOR: Guerrin Marina; Ishigami Akihito; Mechin Marie-Claire; Nachat
Rachida; Valmary Severine; Sebbag Mireille; Simon Michel(a); Senshu
Tatsuo; Serre Guy
AUTHOR ADDRESS: (a)Department of Epidermal Differentiation and Rheumatoid
Autoimmunity, Toulouse-Purpan Pathophysiology Center, INSERM U563 - P.
Sabatier University (IFR30, INSERM-CNRS-P. Sabatier Universite-Centre
Hospitalier Universitaire), 37 Allees J. Guesde, 31073, Toulouse, France
**France E-Mail: msimon@cict.fr
JOURNAL: Biochemical Journal 370 (1):p167-174 15 February 2003 2003
MEDIUM: print
ISSN: 0264-6021
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Peptidylarginine deiminases (PADs) catalyse a
post-translational modification of proteins through the conversion of
arginine residues into citrullines. The existence of four isoforms of PAD
(types I, II, III and IV) encoded by four different genes, which are
distinct in their substrate specificities and tissue-specific expression,
was reported in rodents. In the present study, starting from epidermis
polyadenylated RNA, we cloned by reverse transcriptase-PCR a full-length
cDNA encoding human PAD type I. The cDNA was 2711 bp in length and

encoded a 663-amino-acid sequence. The predicted protein shares 75% identity with the rat PAD type I sequence, but displays only 50-57% identity with the three other known human isoforms. We have described the organization of the human PAD type I gene on chromosome 1p36. A recombinant PAD type I was produced in Escherichia coli and shown to be enzymically active. Human PAD type I mRNAs were detected by reverse transcriptase-PCR not only in the epidermis, but also in various organs, including prostate, testis, placenta, spleen and thymus. In human epidermis extracts, analysed by Western blotting, PAD type I was detected as a 70 kDa polypeptide, in agreement with its predicted molecular mass. As shown by immunohistochemistry, the enzyme was expressed in all the living layers of human epidermis, with the labelling being increased in the granular layer. This is the first description of the human PAD type I gene and the first demonstration of its expression in epidermis.

REGISTRY NUMBERS: 372-75-8: CITRULLINE
DESCRIPTORS:
MAJOR CONCEPTS: Molecular Genetics (Biochemistry and Molecular Biophysics)
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: human (Hominidae)
ORGANISMS: PARTS ETC: chromosome 1--p36; epidermis--integumentary system ; placenta--reproductive system; prostate--reproductive system; spleen--blood and lymphatics, immune system; testis--reproductive system; thymus--blood and lymphatics, endocrine system, immune system
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Humans; Mammals; Primates; Vertebrates
CHEMICALS & BIOCHEMICALS: citrulline; peptidylarginine deiminase type I
GENE NAME: human PAD type I gene (human peptidylarginine deiminase type I gene) (Hominidae)--analysis, expression
METHODS & EQUIPMENT: complementary DNA cloning--genetic techniques, laboratory techniques; gene expression analysis--genetic techniques, laboratory techniques; gene organization analysis--genetic techniques, laboratory techniques
MISCELLANEOUS TERMS: deimination; post-translational modification
CONCEPT CODES:
03502 Genetics and Cytogenetics-General
03508 Genetics and Cytogenetics-Human
10062 Biochemical Studies-Nucleic Acids, Purines and Pyrimidines
10064 Biochemical Studies-Proteins, Peptides and Amino Acids
15002 Blood, Blood-Forming Organs and Body Fluids-Blood and Lymph Studies
15004 Blood, Blood-Forming Organs and Body Fluids-Blood Cell Studies
16504 Reproductive System-Physiology and Biochemistry
17002 Endocrine System-General
17016 Endocrine System-Thymus
18504 Integumentary System-Physiology and Biochemistry
34502 Immunology and Immunochemistry-General; Methods
BIOSYSTEMATIC CODES:
86215 Hominidae

6/9/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12781188 BIOSIS NO.: 200000534811
Human peptidylarginine deiminase type I: Full-length cDNA cloning and expression analysis.
AUTHOR: Guerrin M(a); Ishigami A; Sebbag M(a); Senshu T; Serre G(a

AUTHOR ADDRESS: (a)Department of Biology and Pathology of the Cell, Purpan School of Medicine, INSERM CJF 9602-JFR 30, Toulouse**France
JOURNAL: Journal of Investigative Dermatology 115 (3):p543 September, 2000
MEDIUM: print
CONFERENCE/MEETING: Abstracts for the 30th European Society for Dermatological Research Annual Meeting Berlin, Germany September 21-23, 2000
ISSN: 0022-202X
RECORD TYPE: Citation
LANGUAGE: English
SUMMARY LANGUAGE: English
DESCRIPTORS:
MAJOR CONCEPTS: Molecular Genetics (Biochemistry and Molecular Biophysics); Integumentary System (Chemical Coordination and Homeostasis)
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: human (Hominidae)--normal subjects
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Humans; Mammals; Primates; Vertebrates
CHEMICALS & BIOCHEMICALS: peptidylarginine deiminase type I--epidermal expression analysis, full length complementary DNA cloning
MISCELLANEOUS TERMS: Meeting Abstract
CONCEPT CODES:
03502 Genetics and Cytogenetics-General
00520 General Biology-Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals
03508 Genetics and Cytogenetics-Human
18504 Integumentary System-Physiology and Biochemistry
BIOSYSTEMATIC CODES:
86215 Hominidae

02275443 2003058819
cDNA cloning, gene organization and expression analysis of human peptidylarginine deiminase type I
Guerrin M.; Ishigami A.; Mechin M.-C.; Nachat R.; Valmary S.; Sebbag M.; Simon M.; Senshu T.; Serre G.
ADDRESS: M. Simon, Dept. Epidermal Differentiation/R., INSERM U563 - P. Sabatier Univ., INSERM-CNRS-P. Sabatier Univ.-C., 37 allees J. Guesde, 31073 Toulouse, France
EMAIL: msimon@cict.fr
Journal: Biochemical Journal, 370/1 (167-174), 2003, United Kingdom
PUBLICATION DATE: February 15, 2003
CODEN: BIJOA
ISSN: 0264-6021
DOCUMENT TYPE: Article
LANGUAGES: English SUMMARY LANGUAGES: English
NO. OF REFERENCES: 46

Peptidylarginine deiminases (PADs) catalyse a post-translational modification of proteins through the conversion of arginine residues into citrullines. The existence of four isoforms of PAD (types I, II, III and IV) encoded by four different genes, which are distinct in their substrate specificities and tissue-specific expression, was reported in rodents. In the present study, starting from epidermis polyadenylated RNA, we cloned by reverse transcriptase-PCR a full-length cDNA encoding human PAD type I. The cDNA was 2711 bp in length and encoded a 663-amino-acid sequence. The

predicted protein shares 75% identity with the rat PAD type I sequence, but displays only 50-57% identity with the three other known human isoforms. We have described the organization of the human PAD type I gene on chromosome 1p36. A recombinant PAD type I was produced in Escherichia coli and shown to be enzymically active. Human PAD type I mRNAs were detected by reverse transcriptase-PCR not only in the epidermis, but also in various organs, including prostate, testis, placenta, spleen and thymus. In human epidermis extracts analysed by Western blotting, PAD type I was detected as a 70 kDa polypeptide, in agreement with its predicted molecular mass. As shown by immunohistochemistry, the enzyme was expressed in all the living layers of human epidermis, with the labelling being increased in the granular layer. This is the first description of the human PAD type I gene and the first demonstration of its expression in epidermis.

DESCRIPTORS:
Citrulline; Deimination; Enzyme; Epidermis; Post-translational modification

CLASSIFICATION CODE AND DESCRIPTION:
84.1.3.1 - GENETICS AND MOLECULAR BIOLOGY / MOLECULAR GENETICS / Modification and Restriction / DNA
84.1.13.2 - GENETICS AND MOLECULAR BIOLOGY / MOLECULAR GENETICS / Molecular Biology Techniques / Cloning techniques and PCR
84.5.10.2 - GENETICS AND MOLECULAR BIOLOGY / EUKARYOTIC GENETICS / Human Genetics / Enzymes and other proteins
89.8.7 - CELL AND DEVELOPMENTAL BIOLOGY / DEVELOPMENT (BY TISSUE AND ORGAN SYSTEMS) / Skin and Appendages

MODLECULAR SEQUENCE DATABANK NUMBER:
GENBANK/AB010998/(REFERRED NUMBER)
GENBANK/AB030176/(REFERRED NUMBER)
GENBANK/AB033768/(SUBMITTED NUMBER)
GENBANK/AK026652/(REFERRED NUMBER)
GENBANK/NM013358/(SUBMITTED NUMBER)

6/9/4 (Item 2 from file: 71)
DIALOG(R)File 71:ELSEVIER BIOBASE

01696791 2001069761
The major synovial targets of the rheumatoid arthritis-specific antifilaggrin autoantibodies are deiminated forms of the alpha-and beta-chains of fibrin
Masson-Bessiere C.; Sebbag M.; Girbal-Neuhauser E.; Nogueira L.; Vincent C.
; Senshu T.; Serre G.
ADDRESS: Prof. G. Serre, Lab. de Biol. Cellulaire/Cytologie, Ctr. Hosp. Universitaire Purpan, Place du Dr Baylac, 31059 Toulouse, Cedex, France
EMAIL: serre.g@chu-toulouse.fr
Journal: Journal of Immunology, 166/6 (4177-4184), 2001, United States
PUBLICATION DATE: March 15, 2001
CODEN: JOIMA
ISSN: 0022-1767
DOCUMENT TYPE: Article
LANGUAGES: English SUMMARY LANGUAGES: English
NO. OF REFERENCES: 49

IgG antifilaggrin autoantibodies (AFA) are the most specific serological markers of rheumatoid arthritis. In epithelial tissues, they recognize citrulline-bearing epitopes present on various molecular forms of (pro)filaggrin. Histological analysis of rheumatoid synovial membranes with an Ab to citrulline showed labeling of interstitial amorphous deposits and

mononuclear cells of various types. Immunochemical analysis of exhaustive sequential extracts of the same tissues showed that they contain several deiminated (citrulline containing) proteins. Among them, two proteins, p64-78 and p55-61, present in urea-DTT and guanidine extracts, were shown by immunoblotting to be specifically targeted by AFA. By amino-terminal sequencing the proteins were identifed as deiminated forms of the alpha- and beta-chains of fibrin, respectively. Their identity was confirmed using several Abs specific for the Aalphaand/or to the Bbeta-chain of fibrin(ogen). Moreover, AFA-positive rheumatoid arthritis (RA) sera and purified AFA were highly reactive to the Aalpha- and Bbeta-chains of human fibrlnogen only after deimination of the molecules by a peptidylarginine deiminase. Autoantibodies affinity purified from a pool of RA seca onto deiminated fibrinogen were reactive toward all of the epithelial and synovial targets of AFA. This confirmed that the autoantibodies to the deiminated Aalpha-and Bbeta-chains of fibrinogen, the autoantibodies to the synovial proteins p64-78 and p55-61, and, lastly, AFA, constitute largely overlapping autoantibody populations. These results show that deiminated forms of fibrin deposited in the rheumatoid synovial membranes are the major target of AFA. They suggest that autoimmunization against deiminated fibrin is a critical step in RA pathogenesis.

CLASSIFICATION CODE AND DESCRIPTION:
86.8.5.4 - IMMUNOLOGY AND INFECTIOUS DISEASES / IMMUNE RESPONSE DISORDERS / Autoimmunity / Diagnosis and therapy

6/9/5 (Item 3 from file: 71)
DIALOG(R)File 71:ELSEVIER BIOBASE

01043412 1999010340
The epitopes targeted by the rheumatoid arthritis-associated antifilaggrin autoantibodies are posttranslationally generated on various sites of (pro)filaggrin by deimination of arginine residues
Girbal-Neuhauser E.; Durieux J.-J.; Arnaud M.; Dalbon P.; Sebbag M.; Vincent C.; Simon M.; Senshu T.; Masson-Bessiere C.; Jolivet-Reynaud C.; Jolivet M.; Serre G.
ADDRESS: Prof. G. Serre, Lab. Biol. Cellulaire et Cytologie, Centre Hosp. Universitaire Purpan, Place du Dr Baylac, 31059 Toulouse Cedex, France
EMAIL: serre@cict.fr
Journal: Journal of Immunology, 162/1 (585-594), 1999, United States
PUBLICATION DATE: January 1, 1999
CODEN: JOIMA
ISSN: 0022-1767
DOCUMENT TYPE: Article
LANGUAGES: English SUMMARY LANGUAGES: English
NO. OF REFERENCES: 56

Antifilaggrin autoantibodies (AFA) are a population of IgG autoantibodies associated to rheumatoid arthritis (RA), which includes the so-called 'antikeratin' Abs and antiperinuclear factor. AFA are the most specific serological markers of RA. We previously showed that they recognize human epidermal filaggrin and other profilaggrin-related proteins of various epithelial tissues. Here, we report further characterization of the protein Ags and epitopes targeted by AFA. All the Ags that exhibit numerous neutral/acidic isoelectric variants were immunochemically demonstrated to be deiminated proteins. In vitro deimination of a recombinant human filaggrin by a peptidylarginine deiminase generated AFA epitopes on the protein. Moreover, two of three filaggrin-derived synthetic peptides with a citrulline in the central position were specifically and widely recognized by AFA affinity- purified from a series of RA sera. These

results indicate that citrulline residues are constitutive of the AFA epitopes, but only in the context of specific amino acid sequences of filaggrin. In competition experiments, the two peptides abolished the AFA reactivity of RA sera, showing that they present major AFA epitopes. These data should help in the identification of a putative deiminated AFA-inducing or cross-reactive articular autoantigen and provide new insights into the pathogenesis of RA. They could also open the way toward specific immunosuppressive and/or preventive therapy of RA.

CLASSIFICATION CODE AND DESCRIPTION:
86.8.5.2 - IMMUNOLOGY AND INFECTIOUS DISEASES / IMMUNE RESPONSE DISORDERS / Autoimmunity / Human studies

6/9/6 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

14564273 22458323 PMID: 12416996
cDNA cloning, gene organization and expression analysis of human peptidylarginine deiminase type I.
Guerrin Marina; Ishigami Akihito; Mechin Marie-Claire; Nachat Rachida; Valmary Severine; Sebbag Mireille; Simon Michel; Senshu Tatsuo; Serre Guy
Department of Epidermal Differentiation and Rheumatoid Autoimmunity, Toulouse-Purpan Pathophysiology Center, INSERM U563 - P. Sabatier University (IFR30, INSERM-CNRS-P. Sabatier Universite-Centre Hospitalier Universitaire), Toulouse, France.
Biochemical journal (England) Feb 15 2003, 370 (Pt 1) p167-74, ISSN 0264-6021 Journal Code: 2984726R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Peptidylarginine deiminases (PADs) catalyse a post-translational modification of proteins through the conversion of arginine residues into citrullines. The existence of four isoforms of PAD (types I, II, III and IV) encoded by four different genes, which are distinct in their substrate specificities and tissue-specific expression, was reported in rodents. In the present study, starting from epidermis polyadenylated RNA, we cloned by reverse transcriptase-PCR a full-length cDNA encoding human PAD type I. The cDNA was 2711 bp in length and encoded a 663-amino-acid sequence. The predicted protein shares 75% identity with the rat PAD type I sequence, but displays only 50-57% identity with the three other known human isoforms. We have described the organization of the human PAD type I gene on chromosome 1p36. A recombinant PAD type I was produced in Escherichia coli and shown to be enzymically active. Human PAD type I mRNAs were detected by reverse transcriptase-PCR not only in the epidermis, but also in various organs, including prostate, testis, placenta, spleen and thymus. In human epidermis extracts analysed by Western blotting, PAD type I was detected as a 70 kDa polypeptide, in agreement with its predicted molecular mass. As shown by immunohistochemistry, the enzyme was expressed in all the living layers of human epidermis, with the labelling being increased in the granular layer. This is the first description of the human PAD type I gene and the first demonstration of its expression in epidermis.
Tags: Human; Support, Non-U.S. Gov't
Descriptors: *Hydrolases--genetics--GE; Amino Acid Sequence; Cloning, Molecular; DNA, Complementary; Epidermis--enzymology--EN; Hydrolases --chemistry--CH; Hydrolases--metabolism--ME; Molecular Sequence Data; RNA, Messenger--genetics--GE; Recombinant Proteins--chemistry--CH; Recombinant Proteins--genetics--GE; Recombinant Proteins--metabolism--ME; Sequence

Homology, Amino Acid; Substrate Specificity
Molecular Sequence Databank No.: GENBANK/AB033768; GENBANK/NM013358
CAS Registry No.: 0 (DNA, Complementary); 0 (RNA, Messenger); 0 (Recombinant Proteins)
Enzyme No.: EC 3. (Hydrolases); EC 3.5.3.- (peptidylarginine deiminase type I)
Record Date Created: 20030206
Record Date Completed: 20030314

6/9/7 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

14506460 22458323 PMID: 12416996
cDNA cloning, gene organization and expression analysis of human peptidylarginine deiminase type I.
Guerrin Marina; Ishigami Akihito; Mechin Marie-Claire; Nachat Rachida; Valmary Severine; Sebbag Mireille; Simon Michel; Senshu Tatsuo; Serre Guy
Department of Epidermal Differentiation and Rheumatoid Autoimmunity, Toulouse-Purpan Pathophysiology Center, INSERM U563 - P. Sabatier University (IFR30, INSERM-CNRS-P. Sabatier Universite-Centre Hospitalier Universitaire), Toulouse, France.
Biochemical journal (England) Feb 15 2003, 370 (Pt 1) p167-74, ISSN 0264-6021 Journal Code: 2984726R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Process
Subfile: INDEX MEDICUS
Peptidylarginine deiminases (PADs) catalyse a post-translational modification of proteins through the conversion of arginine residues into citrullines. The existence of four isoforms of PAD (types I, II, III and IV) encoded by four different genes, which are distinct in their substrate specificities and tissue-specific expression, was reported in rodents. In the present study, starting from epidermis polyadenylated RNA, we cloned by reverse transcriptase-PCR a full-length cDNA encoding human PAD type I. The cDNA was 2711 bp in length and encoded a 663-amino-acid sequence. The predicted protein shares 75% identity with the rat PAD type I sequence, but displays only 50-57% identity with the three other known human isoforms. We have described the organization of the human PAD type I gene on chromosome 1p36. A recombinant PAD type I was produced in Escherichia coli and shown to be enzymically active. Human PAD type I mRNAs were detected by reverse transcriptase-PCR not only in the epidermis, but also in various organs, including prostate, testis, placenta, spleen and thymus. In human epidermis extracts analysed by Western blotting, PAD type I was detected as a 70 kDa polypeptide, in agreement with its predicted molecular mass. As shown by immunohistochemistry, the enzyme was expressed in all the living layers of human epidermis, with the labelling being increased in the granular layer. This is the first description of the human PAD type I gene and the first demonstration of its expression in epidermis.
Molecular Sequence Databank No.: GENBANK/AB033768; GENBANK/NM013358
Record Date Created: 20030206

6/9/8 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11666499 99101527 PMID: 9886436
The epitopes targeted by the rheumatoid arthritis-associated

antifilaggrin autoantibodies are posttranslationally generated on various sites of (pro)filaggrin by deimination of arginine residues.

Girbal-Neuhauser E; Durieux J J; Arnaud M; Dalbon P; Sebbag M; Vincent C; Simon M; Senshu T; Masson-Bessiere C; Jolivet-Reynaud C; Jolivet M; Serre G

Department of Biology and Pathology of the Cell, Institut National de la Sante et de la Recherche Medicale, Toulouse-Purpan School of Medicine, University Toulouse III, France.

Journal of immunology (Baltimore, Md. - 1950) (UNITED STATES) Jan 1 1999, 162 (1) p585-94, ISSN 0022-1767 Journal Code: 2985117R

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: AIM; INDEX MEDICUS

Antifilaggrin autoantibodies (AFA) are a population of IgG autoantibodies associated to rheumatoid arthritis (RA), which includes the so-called "antikeratin" Abs and antiperinuclear factor. AFA are the most specific serological markers of RA. We previously showed that they recognize human epidermal filaggrin and other profilaggrin-related proteins of various epithelial tissues. Here, we report further characterization of the protein Ags and epitopes targeted by AFA. All the Ags that exhibit numerous neutral/ acidic isoelectric variants were immunochemically demonstrated to be deiminated proteins. In vitro deimination of a recombinant human filaggrin by a peptidylarginine deiminase generated AFA epitopes on the protein. Moreover, two of three filaggrin-derived synthetic peptides with a citrulline in the central position were specifically and widely recognized by AFA affinity-purified from a series of RA sera. These results indicate that citrulline residues are constitutive of the AFA epitopes, but only in the context of specific amino acid sequences of filaggrin. In competition experiments, the two peptides abolished the AFA reactivity of RA sera, showing that they present major AFA epitopes. These data should help in the identification of a putative deiminated AFA-inducing or cross-reactive articular autoantigen and provide new insights into the pathogenesis of RA. They could also open the way toward specific immunosuppressive and/or preventive therapy of RA.

Tags: Human; Support, Non-U.S. Gov't

Descriptors: *Arginine--metabolism--ME; *Arthritis, Rheumatoid --immunology--IM; *Autoantibodies--biosynthesis--BI; *Epitopes--metabolism --ME; *Intermediate Filament Proteins--immunology--IM; *Protein Precursors --immunology--IM; *Protein Processing, Post-Translational--immunology--IM; Amino Acid Sequence; Amino Acid Substitution; Arthritis, Rheumatoid--blood --BL; Arthritis, Rheumatoid--metabolism--ME; Autoantibodies--blood--BL; Autoantibodies--metabolism--ME; Citrulline--metabolism--ME; Epidermis --immunology--IM; Epithelium--immunology--IM; Epithelium--metabolism--ME; Hydrolases--metabolism--ME; Intermediate Filament Proteins--genetics--GE; Intermediate Filament Proteins--metabolism--ME; Molecular Sequence Data; Peptide Fragments--chemical synthesis--CS; Peptide Fragments--immunology --IM; Peptide Fragments--metabolism--ME; Protein Precursors--genetics--GE; Protein Precursors--metabolism--ME; Recombinant Proteins--immunology--IM; Recombinant Proteins--metabolism--ME

Molecular Sequence Databank No.: GENBANK/AF043380

CAS Registry No.: 0 (Autoantibodies); 0 (Epitopes); 0 (Intermediate Filament Proteins); 0 (Peptide Fragments); 0 (Protein Precursors); 0 (Recombinant Proteins); 0 (filaggrin); 0 (profilaggrin); 372-75-8 (Citrulline); 74-79-3 (Arginine)

Enzyme No.: EC 3. (Hydrolases); EC 3.5.3.15 (protein-arginine deiminase)

Record Date Created: 19990121

Record Date Completed: 19990121

6/9/9 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09373715 21136399 PMID: 11238669

The major synovial targets of the rheumatoid arthritis-specific antifilaggrin autoantibodies are deiminated forms of the alpha- and beta-chains of fibrin.

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Journal of immunology (Baltimore, Md. - 1950) (United States) Mar 15 2001, 166 (6) p4177-84, ISSN 0022-1767 Journal Code: 2985117R

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: AIM; INDEX MEDICUS

IgG antifilaggrin autoantibodies (AFA) are the most specific serological markers of rheumatoid arthritis. In epithelial tissues, they recognize citrulline-bearing epitopes present on various molecular forms of (pro)filaggrin. Histological analysis of rheumatoid synovial membranes with an Ab to citrulline showed labeling of interstitial amorphous deposits and mononuclear cells of various types. Immunochemical analysis of exhaustive sequential extracts of the same tissues showed that they contain several deiminated (citrulline containing) proteins. Among them, two proteins, p64--78 and p55--61, present in urea-DTT and guanidine extracts, were shown by immunoblotting to be specifically targeted by AFA. By amino-terminal sequencing the proteins were identified as deiminated forms of the alpha- and beta-chains of fibrin, respectively. Their identity was confirmed using several Abs specific for the A alpha- and/or to the B beta-chain of fibrin(ogen). Moreover, AFA-positive rheumatoid arthritis (RA) sera and purified AFA were highly reactive to the A alpha- and B beta-chains of human fibrinogen only after deimination of the molecules by a peptidylarginine deiminase . Autoantibodies affinity purified from a pool of RA sera onto deiminated fibrinogen were reactive toward all of the epithelial and synovial targets of AFA. This confirmed that the autoantibodies to the deiminated A alpha-and B beta-chains of fibrinogen, the autoantibodies to the synovial proteins p64--78 and p55--61, and, lastly, AFA, constitute largely overlapping autoantibody populations. These results show that deiminated forms of fibrin deposited in the rheumatoid synovial membranes are the major target of AFA. They suggest that autoimmunization against deiminated fibrin is a critical step in RA pathogenesis.

Tags: Animal; Human; Support, Non-U.S. Gov't

Descriptors: *Arthritis, Rheumatoid--immunology--IM; *Autoantibodies --metabolism--ME; *Autoantigens--immunology--IM; *Fibrin--metabolism--ME; *Imines--metabolism--ME; *Intermediate Filament Proteins--immunology--IM; *Synovial Membrane--immunology--IM; Antigen-Antibody Reactions; Arthritis, Rheumatoid--pathology--PA; Autoantigens--chemistry--CH; Autoantigens --metabolism--ME; Epitopes--immunology--IM; Epitopes--metabolism--ME; Fibrin--chemistry--CH; Fibrin--immunology--IM; Fibrinogen--chemistry--CH; Fibrinogen--immunology--IM; Fibrinogen--metabolism--ME; Immunohistochemis try; Intermediate Filament Proteins--chemistry--CH; Intermediate Filament Proteins--metabolism--ME; Peptide Fragments--chemistry--CH; Peptide Fragments--immunology--IM; Peptide Fragments--metabolism--ME; Rats; Synovial Membrane--chemistry--CH; Synovial Membrane--metabolism--ME

CAS Registry No.: 0 (Autoantibodies); 0 (Autoantigens); 0 (Epitopes) ; 0 (Imines); 0 (Intermediate Filament Proteins); 0 (Peptide

Fragments); 0 (filaggrin); 9001-31-4 (Fibrin); 9001-32-5 (Fibrinogen)
Record Date Created: 20010312
Record Date Completed: 20010517

6/9/10 (Item 1 from file: 172)
DIALOG(R)File 172:EMBASE Alert

02896157 EMBASE No: 2003094195
cDNA cloning, gene organization and expression analysis of human peptidylarginine deiminase type I
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Biochemical Journal (United Kingdom) 2003 VOL/ISS/PG: 370/1 (167-174)
CODEN: BIJOA ISSN: 0264-6021
PUBLICATION DATE: 20030215
DOCUMENT TYPE: Article
NUMBER OF REFERENCES: 46
LANGUAGES: ENGLISH SUMMARY LANGUAGES: ENGLISH

Peptidylarginine deiminases (PADs) catalyse a post-translational modification of proteins through the conversion of arginine residues into citrullines. The existence of four isoforms of PAD (types I, II, III and IV) encoded by four different genes, which are distinct in their substrate specificities and tissue-specific expression, was reported in rodents. In the present study, starting from epidermis polyadenylated RNA, we cloned by reverse transcriptase-PCR a full-length cDNA encoding human PAD type I. The cDNA was 2711 bp in length and encoded a 663-amino-acid sequence. The predicted protein shares 75% identity with the rat PAD type I sequence, but displays only 50-57% identity with the three other known human isoforms. We have described the organization of the human PAD type I gene on chromosome 1p36. A recombinant PAD type I was produced in Escherichia coli and shown to be enzymically active. Human PAD type I mRNAs were detected by reverse transcriptase-PCR not only in the epidermis, but also in various organs, including prostate, testis, placenta, spleen and thymus. In human epidermis extracts analysed by Western blotting, PAD type I was detected as a 70 kDa polypeptide, in agreement with its predicted molecular mass. As shown by immunohistochemistry, the enzyme was expressed in all the living layers of human epidermis, with the labelling being increased in the granular layer. This is the first description of the human PAD type I gene and the first demonstration of its expression in epidermis.
AUTHOR KEYWORDS: Citrulline; Deimination; Enzyme; Epidermis; Post-translational modification